JOURNAL OF PHARMACOKINETICS AND BIOPHARMACEUTICS

Volume 9, 1981

A journal devoted to illustrating the importance of pharmacokinetic and biopharmaceutical applications in the understanding of drug action, design, therapy, and evaluation. Experimental and theoretical papers deal with kinetics of drug disposition; clinical pharmacokinetics; time course of pharmacological response; factors affecting formation and disposition of drug metabolites; studies in drug release from dosage forms; dosage form developments and their evaluation in animals and man; bioavailability studies—*in vitro* and *in vivo* correlations; and application of computers to pharmacokinetic analysis. All papers show some correlation with data describing the time course of drug disposition or action, or both, in animals and man.

FOUNDING EDITOR (1973–1981)
Sidney Riegelman

EDITORS
Leslie Z. Benet
Professor of Pharmacy and Pharmaceutical Chemistry, School of Pharmacy, University of California, San Francisco, California

Malcolm Rowland
Professor of Pharmacy, Department of Pharmacy, The University, Manchester, Manchester, England

ASSOCIATE EDITOR
Svein Øie
Assistant Professor of Pharmacy and Pharmaceutical Chemistry, School of Pharmacy, University of California, San Francisco, California

CONSULTING EDITORS
D. D. Breimer, University of Leiden, Leiden, The Netherlands
E. R. Garrett, University of Florida, Gainesville, Florida
M. Gibaldi, University of Washington, Seattle, Washington
T. Higuchi, University of Kansas, Lawrence, Kansas
G. Levy, State University of New York, Buffalo, New York
G. Segre, University of Siena, Siena, Italy
T. Teorell, Institute of Physiology and Medical Biophysics, Uppsala, Sweden
J. G. Wagner, University of Michigan, Ann Arbor, Michigan

EDITORIAL ADVISORY BOARD
K. B. Bischoff, University of Delaware, Newark, Delaware
R. L. Dedrick, National Institutes of Health, Bethesda, Maryland
L. Dettli, Medizinische Universitätsklinik, Basel, Switzerland
F. H. Dost, Universitäts-Kinderklinik, Giessen, West Germany
M. Hanano, University of Tokyo, Tokyo, Japan
J. Hirtz, Ciba-Geigy, Rueil-Malmaison, France
W. J. Jusko, State University of New York, Buffalo, New York
S. A. Kaplan, Hoffmann-La Roche, Nutley, New Jersey
K. C. Kwan, Merck, Sharp and Dohme Research Laboratories, West Point, Pennsylvania
C. M. Metzler, The Upjohn Company, Kalamazoo, Michigan
L. K. Paalzow, Apoteksbolaget AB, Solna, Sweden
H. Sezaki, Kyoto University, Kyoto, Japan
L. B. Sheiner, University of California, San Francisco, California
G. T. Tucker, University of Sheffield, Sheffield, England
J. van Rossum, University of Nijmegen, Nijmegen, The Netherlands
W. J. Westlake, Smith Kline and French Laboratories, Philadelphia, Pennsylvania
G. Wilkinson, Vanderbilt University, Nashville, Tennessee

Published bimonthly at Winterstoke Road, Bristol 3, England, by Plenum Publishing Corporation, 233 Spring Street, New York, N.Y. 10013. In 1981, Volume 9 (6 issues) will be published. Subscription orders should be addressed to the publisher. *Journal of Pharmacokinetics and Biopharmaceutics* is abstracted or indexed in Beck Medical Information, Biological Abstracts, Chemical Abstracts, Current Contents, Excerpta Medica, Index Medicus, International Abstracts of Biological Sciences, International Pharmaceutical Abstracts, Referativnyi Zhurnal, and Science Citation Index.

© 1981 Plenum Publishing Corporation. *Journal of Pharmacokinetics and Biopharmaceutics* participates in the program of Copyright Clearance Center, Inc. The appearance of a code line at the bottom of the first page of an article in the journal indicates the copyright owner's consent that copies of the article may be made for personal or internal use. However, this consent is given on the condition that the copier pay the stated per-copy fee through the Copyright Clearance Center, Inc. for all copying not explicitly permitted by Sections 107 or 108 of the U.S. Copyright Law. It does not extend to other kinds of copying, such as copying for general distribution, for advertising or promotional purposes, for creating new collective works, or for resale, nor to the reprinting of figures, tables and text excerpts.

Subscription rates:

Volume 9, 1981 (6 issues) $94.00 (outside the U.S., $106.00). Price for individual subscribers certifying that the journal is for their personal use, $47.00 (outside the U.S., $55.00).

Volume 10, 1982 (6 issues) $110.00 (outside the U.S., $124.00). Price for individual subscribers certifying that the journal is for their personal use, $47.00 (outside the U.S., $55.00).

Second-class postage paid at Jamaica, N.Y. 11431.

Printed in Great Britain.

Journal of Pharmacokinetics and Biopharmaceutics is published bimonthly at Winterstoke Road, Bristol 3, England, by Plenum Publishing Corporation, 233 Spring Street, New York, N.Y. 10013. In 1981, Volume 9 (6 issues) will be published. Subscription orders should be addressed to the publisher. *Journal of Pharmacokinetics and Biopharmaceutics* is abstracted or indexed in Biological Abstracts, Chemical Abstracts, Current Contents, Excerpta Medica, Index Medicus, International Abstracts of Biological Sciences, International Pharmaceutical Abstracts, Referativnyi Zhurnal, and Science Citation Index. © 1981 Plenum Publishing Corporation. *Journal of Pharmacokinetics and Biopharmaceutics* participates in the program of Copyright Clearance Center, Inc. The appearance of a code line at the bottom of the first page of an article in this journal indicates the copyright owner's consent that copies of the article may be made for personal or internal use. However, this consent is given on the condition that the copier pay the stated per-copy fee through the Copyright Clearance Center. Inc. for all copying not explicitly permitted by Sections 107 or 108 of the U.S. Copyright Law. It does not extend to other kinds of copying, such as copying for general distribution, for advertising or promotional purposes, for creating new collective works, or for resale, nor to the reprinting of figures, tables, and text excerpts.

Another journal from Plenum

Journal of Pharmacokinetics and Biopharmaceutics

Vol. 9, No. 1 **February 1981**

CONTENTS

Effect of Smoking on Prednisone, Prednisolone, and Dexamethasone Pharmacokinetics 1
James Q. Rose, Anthony M. Yurchak, A. Wayne Meikle, and William J. Jusko

Influence of Plasma Protein Binding Kinetics on Hepatic Clearance Assessed from a "Tube" Model and a "Well-Stirred" Model 15
Jens Aa. Jansen

An Analytical Pharmacodynamic Model for Nondepolarizing Neuromuscular Blocking Agents 27
Alain d'Hollander and Claude Delcroix

Continuous Transepidermal Drug Collection: Basis for Use in Assessing Drug Intake and Pharmacokinetics 41
Carl C. Peck, Kenneth Lee, and Charles E. Becker

PHARMACOKINETIC DATA

A Standard Approach to Compiling Clinical Pharmacokinetic Data 59
Lewis B. Sheiner, Leslie Z. Benet, and Louis A. Pagliaro

MEETING ANNOUNCEMENT 129

Journal of Pharmacokinetics and Biopharmaceutics

Vol. 9, No. 2 **April 1981**

CONTENTS

Predicting Individual Phenytoin Dosage 131
Samuel Vozeh, Keith T. Muir, Lewis B. Sheiner, and Ferenc Follath

Evidence of Nonlinearity in Digoxin Pharmacokinetics 147
J. G. Wagner, K. D. Popat, S. K. Das, E. Sakmar, and H. Movahhed

Analysis of the Contributions of Permeability and Flow to Intercompartmental Clearance 167
G. Paul Stec and Arthur J. Atkinson, Jr.

Kinetics of Drug Displacement Interactions 181
Leon J. Aarons and Malcolm Rowland

Intestinal Absorption-Partition Relationships: A Tentative Functional Nonlinear Model 191
José M. Plá-Delfina and Joaquín Moreno

Properties of the Recirculation Model: Matrix Description and Conditions for a Monotonic Decreasing Single Pass Response 217
David J. Cutler

Properties of the Recirculation Model: Calculation of the Amount of Drug in the Body from Blood Concentration Data, with Application to Absorption Rate Calculations 225
David J. Cutler

An Aid to Decision-Making in Bioequivalence Assessment 235
H. Fluehler, J. Hirtz, and H. A. Moser

Journal of Pharmacokinetics and Biopharmaceutics

Vol. 9, No. 3 **June 1981**

CONTENTS

Evidence that Cannabidiol Does Not Significantly Alter the Pharmacokinetics of Tetrahydrocannabinol in Man 245
C. Anthony Hunt, Reese T. Jones, Ronald I. Herning, and John Bachman

A New Blood-Flow Pharmacokinetic Model for Ethanol 261
Jay L. Rheingold, Richard E. Lindstrom, and Paul K. Wilkinson

Arterial-Venous Blood Alcohol Concentration Gradients 279
Paul K. Wilkinson and Jay L. Rheingold

Enteric Transport of Chlordecone (Kepone®) in the Rat 309
Peter M. Bungay, Robert L. Dedrick, and H. B. Matthews

The Pharmacokinetics of the Intravenous Steroid Anesthetic Alphaxalone in the Isolated Perfused Rat Lung 343
Michael E. Jones and Terence E. Nicholas

Pharmacokinetics of Digoxin in the Turkey and Comparison with Other Species 357
Eunna Park, Stanley Einzig, Nancy A. Staley, and George R. Noren

Simultaneous Pharmacokinetic and Pharmacodynamic Modeling 367
Wayne A. Colburn

Journal of Pharmacokinetics and Biopharmaceutics

Vol. 9, No. 4 **August 1981**

CONTENTS

Dose Dependent Pharmacokinetics of Prednisone and Prednisolone in Man 389
James Q. Rose, Anthony M. Yurchak, and William J. Jusko

Pharmacokinetics of Propranolol 419
Lars Borgström, Carl-Gustav Johansson, Hans Larsson, and Rune Lenander

Pharmacokinetics of Bendroflumethiazide After Low Oral Doses 431
Lars Borgström, Carl-Gustav Johansson, Hans Larsson, and Rune Lenander

Effects of pH on the Accumulation of Sulfonamides by Fish 443
I-Hui Lo and William L. Hayton

Saturable Kinetics of Intravenous Chlorothiazide in the Rhesus Monkey 461
Jo H. Gustafson and Leslie Z. Benet

Metabolite Pharmacokinetics: The Area Under the Curve of Metabolite and the Fractional Rate of Metabolism of a Drug After Different Routes of Administration for Renally and Hepatically Cleared Drugs and Metabolites 477
K. Sandy Pang

Metabolite to Parent Drug Concentration Ratio as a Function of Parent Drug Extraction Ratio: Cases of Nonportal Route of Administration 489
Elizabeth A. Lane and René H. Levy

The Efficient Use of NONLIN for Unbalanced Multiple Dose Data 497
Gary L. Elfring and Carl M. Metzler

SCIENTIFIC COMMENTARY

Some Suggestions for Measuring Predictive Performance 503
Lewis B. Sheiner and Stuart L. Beal

MEETING ANNOUNCEMENT 513

Journal of Pharmacokinetics and Biopharmaceutics

Vol. 9, No. 5 **October 1981**

CONTENTS

In Memoriam: Sidney Riegelman (1921–1981) 515

Physiologic Model for the Pharmacokinetics of 2′Deoxycoformycin in Normal and Leukemic Mice 519
Franklin G. King and Robert L. Dedrick

Pharmacokinetic Study of Sisomicin in Humans 535
Menger Chung, John J. Schrogie, and Samson Symchowicz

Pharmacokinetics of 2-Butanol and its Metabolites in the Rat 553
F. K. Dietz, M. Rodriguez-Giaxola, G. J. Traiger, V. J. Stella, and K. J. Himmelstein

Development and Identification of a Multicompartment Model for the Distribution of Adriamycin in the Rat 577
P. Sonneveld and J. A. Mulder

The Pharmacokinetics of Penicillamine in a Female Mongrel Dog 603
Richard F. Bergstrom, Donald R. Kay, and John G. Wagner

Variability in Derived Parameters of Furosemide Pharmacokinetics 623
Polavat Chennavasin, Robert A. Johnson, and D. Craig Brater

Evaluation of Methods for Estimating Population Pharmacokinetic Parameters II. Biexponential Model and Experimental Pharmacokinetic Data 635
Lewis B. Sheiner and Stuart L. Beal

Journal of Pharmacokinetics and Biopharmaceutics

Vol. 9, No. 6 **December 1981**

CONTENTS

A Physiologically Based Pharmacokinetic Model for the Intraocular Distribution of Pilocarpine in Rabbits 653
Susan C. Miller, Kenneth J. Himmelstein, and Thomas F. Patton

Clinical Bioavailability Evaluation of a Controlled Release Formulation of Diazepam 679
Jo H. Gustafson, Lester Weissman, Robert E. Weinfeld, Alice A. Holazo, Ko-Chin Khoo, and Stanley A. Kaplan

A Linear Model of Reversible Metabolism and Its Application to Bioavailability Assessment 693
S. Hwang, K. C. Kwan, and K. S. Albert

Pharmacokinetics and Tissue Distribution of Chlorpheniramine in Rabbits after Intravenous Administration 711
Shiew-Mei Huang and Win L. Chiou

Oral Absorption and Presystemic First-Pass Effect of Chlorpheniramine in Rabbits 725
Shiew-Mei Huang, Yih-Chain Huang, and Win L. Chiou

Optimal Sampling Times for Pharmacokinetic Experiments 739
David Z. D'Argenio

MEETING ANNOUNCEMENT 757
Author Index to Volume 9 759
Subject Index to Volume 9 761